CLAIMS

1. A compound of formula I:

$$A \longrightarrow Ar^{1} \longrightarrow Ar^{2}$$

5 wherein:

20

25

A is a moiety of formula II:

$$(CH_2)_a$$
 $(CH_2)_b$
 $(CH_2)_c$
 $(CH_2)_c$

D is oxygen or sulfur;

E is a single bond, oxygen, sulfur, or NR³;

Ar¹ is a 5- or 6-membered aromatic heterocyclic ring having 1, 2 or 3 heteroatoms selected from nitrogen, oxygen or sulfur where not more than one of said heteroatoms is oxygen or sulfur, or

Ar¹ is phenyl;

Ar² is a 5- or 6-membered aromatic heterocyclic ring having 1, 2 or 3 heteroatoms selected from nitrogen, oxygen or sulfur where not more than one of said heteroatoms is oxygen or sulfur, or

Ar² is phenyl, or

Ar² is an 8- or 9-, or 10-membered fused aromatic carbocyclic ring or fused aromatic heterocyclic ring having 1, 2 or 3 heteroatoms selected from nitrogen, oxygen or sulfur where not more than one of said heteroatoms is oxygen or sulfur, or an 8- or 9-, or 10-membered aromatic carbocyclic ring;

the rings Ar¹ and Ar² are substituted with 0, 1, 2 or 3 substituents selected from: halogen, C_{1.4}alkyl, C_{2.4}alkenyl, C_{2.4}alkynyl, CN, NO₂, CF₃ NR¹R², CH₂NR¹R², OR², CH₂OR² or CO₂R³;

R¹ and R² at each occurrence are independently selected from hydrogen, C₁₋₄alkyl, aryl, heteroaryl, C(O)R³, C(O)NHR³, CO₂R³ or SO₂R³, or

 R^1 and R^2 in combination is -(CH₂)_jG(CH₂)_k- wherein G is oxygen, sulfur, NR³, or a bond;

a, b and c are each 1 or 2;

j is 2, 3 or 4;

5 k is 0, 1 or 2, and

 R^3 at each occurrence is independently selected from hydrogen, C_{1-4} alkyl, aryl, or heteroaryl;

or a diastereoisomer, enantiomer or pharmaceutically-acceptable salt thereof.

- 10 2. A compound according to Claim 1, wherein D is oxygen.
 - 3. A compound according to Claim 2, wherein E is a single bond.
 - 4. A compound according to Claim 2, wherein E is oxygen or NR³.

15

5. A compound according to Claim 1, wherein A is



 Π

or a diastereoisomer, enantiomer or pharmaceutically-acceptable salt thereof.

20 6. A compound of Claim 1, wherein

Ar¹ is a 5- or 6-membered aromatic heterocyclic ring having 1 or 2 heteroatoms selected from nitrogen, oxygen or sulfur where not more than one of said heteroatoms is oxygen or sulfur, or

Ar¹ is phenyl,

- or a diastereoisomer, enantiomer or pharmaceutically-acceptable salt thereof.
 - 7. A compound according to Claim 6 wherein Ar¹ is a benzene ring, furan ring or thiophene ring.

8. A compound according to Claim 1, wherein

Ar² is a 5- or 6-membered aromatic heterocyclic ring having 1 or 2 heteroatoms selected from nitrogen, oxygen or sulfur where not more than one of said heteroatoms is oxygen or sulfur, or a phenyl,

- 5 or a diastereoisomer, enantiomer or pharmaceutically-acceptable salt thereof.
 - 9. A compound according to Claim 8, wherein Ar² is a benzene ring, furan ring, thiophene ring, or pyridine ring.
- 10 10. A compound according to Claim 1, wherein
 the -EAr² and the C(=D)A moieties on Ar¹ are positioned in a 1,3-relationship relative
 to each other;
 or a diastereoisomer, enantiomer or pharmaceutically-acceptable salt thereof.
- 11. A compound according to Claim 1, wherein Ar¹ or Ar² is substituted with 0 or 1 substituents selected from: halogen, C₁₋₄alkyl, C₂₋₄alkenyl, C₂₋₄alkynyl, CN, NO₂, NR¹R², CH₂NR¹R², OR³, CH₂OR³, CO₂R³ or CF₃; or a diastereoisomer, enantiomer or pharmaceutically-acceptable salt thereof.
- 20 12. A compound according to Claim 1, wherein A is a moiety of formula II:



D

D is oxygen;

E is a single bond;

Ar¹ is a 5- or 6-membered aromatic heterocyclic ring having 1, 2 or 3 heteroatoms

25 selected from nitrogen, oxygen or sulfur where not more than 1 of said heteroatoms is oxygen or sulfur, or

Ar¹ is phenyl

WO 2004/016617 PCT/SE2003/001277

Ar² is a 5- or 6-membered aromatic heterocyclic ring having 1, 2 or 3 heteroatoms selected from nitrogen, oxygen or sulfur where not more than 1 of said heteroatoms is oxygen or sulfur, or

Ar² is phenyl,

- 5 or a diastereoisomer, enantiomer or pharmaceutically-acceptable salt thereof.
 - 13. A compound of Claim 12, wherein Ar¹ is a benzene ring, furan ring or thiophene ring.
- 14. A compound according to Claim 1, having the groups -EAr² and -C(=O)A, positioned in a 1,3-relationship relative to each other and wherein Ar² has 0 or 1 substituents selected from: halogen, C₁₋₄alkyl, C₂₋₄alkenyl, C₂₋₄alkynyl, CN, NO₂, NR¹R², CH₂NR¹R², OR¹, CH₂OR¹, CO₂R³ or CF₃; or a diastereoisomer, enantiomer or pharmaceutically-acceptable salt thereof.
- 15 15. A compound according to Claim 1, selected from:
 - (1,4-diazabicyclo[3.2.2]non-4-yl)(biphenyl-3-yl)methanone;
 - (1,4-diazabicyclo[3.2.2]non-4-yl)(3-(2-pyridyl)phenyl)methanone;
 - (1,4-diazabicyclo[3.2.2]non-4-yl)(3-(3-pyridyl)phenyl)methanone;
 - (1,4-diazabicyclo[3.2.2]non-4-yl)(3-(4-pyridyl)phenyl)methanone;
- 20 (1,4-diazabicyclo[3.2.2]non-4-yl)(3-(furan-2-yl)phenyl)methanone;
 - (1,4-diazabicyclo[3.2.2]non-4-yl)(3-(furan-3-yl)phenyl)methanone;
 - (1,4-diazabicyclo[3.2.2]non-4-yl)(3-(thiophen-2-yl)phenyl)methanone;
 - (1,4-diazabicyclo[3.2.2]non-4-yl)(3-(thiophen-3-yl)phenyl)methanone;
 - (1,4-diazabicyclo[3.2.2]non-4-yl)(biphenyl-4-yl)methanone;
- 25 (1,4-diazabicyclo[3.2.2]non-4-yl)(4-(2-pyridyl)phenyl)methanone;
 - (1,4-diazabicyclo[3.2.2]non-4-yl)(4-(3-pyridyl)phenyl)methanone;
 - (1,4-diazabicyclo[3.2.2]non-4-yl)(4-(4-pyridyl)phenyl)methanone;
 - (1,4-diazabicyclo[3.2.2]non-4-yl)(4-(furan-2-yl)phenyl)methanone;
 - (1,4-diazabicyclo[3.2.2]non-4-yl)(4-(furan-3-yl)phenyl)methanone;
- 30 (1,4-diazabicyclo[3.2.2]non-4-yl)(4-(thiophen-2-yl)phenyl)methanone;
 - (1,4-diazabicyclo[3.2.2]non-4-yl)(4-(thiophen-3-yl)phenyl)methanone;
 - (1,4-diazabicyclo[3.2.2]non-4-yl)(5-phenylfuran-2-yl)methanone;

- (1,4-diazabicyclo[3.2.2]non-4-yl)(5-(2-pyridyl)furan-2-yl)methanone;
- (1,4-diazabicyclo[3.2.2]non-4-yl)(5-(3-pyridyl)furan-2-yl)methanone;
- (1,4-diazabicyclo[3.2.2]non-4-yl)(5-(4-pyridyl)furan-2-yl)methanone;
- (1,4-diazabicyclo[3.2.2]non-4-yl)(5-(furan-2-yl)furan-2-yl)methanone;
- 5 (1,4-diazabicyclo[3.2.2]non-4-yl)(5-(furan-3-yl)furan-2-yl)methanone;
 - (1.4-diazabicyclo[3.2.2]non-4-yl)(5-(thiophen-2-yl)furan-2-yl)methanone;
 - (1,4-diazabicyclo[3.2.2]non-4-yl)(5-(thiophen-3-yl)furan-2-yl)methanone;
 - (1,4-diazabicyclo[3.2.2]non-4-yl)(2-phenylthiophen-4-yl)methanone;
 - (1,4-diazabicyclo[3,2,2]non-4-yl)(2-(2-pyridyl)thiophen-4-yl)methanone;
- 10 (1,4-diazabicyclo[3.2.2]non-4-yl)(2-(3-pyridyl)thiophen-4-yl)methanone;
 - (1,4-diazabicyclo[3.2.2]non-4-yl)(2-(4-pyridyl)thiophen-4-yl)methanone;
 - (1,4-diazabicyclo[3.2.2]non-4-yl)(2-(furan-2-yl)thiophen-4-yl)methanone;
 - (1,4-diazabicyclo[3.2.2]non-4-yl)(2-(furan-3-yl)thiophen-4-yl)methanone;
 - (1,4-diazabicyclo[3.2.2]non-4-yl)(2-(thiophen-2-yl)thiophen-4-yl)methanone;
- 15 (1,4-diazabicyclo[3.2.2]non-4-yl)(2-(thiophen-3-yl)thiophen-4-yl)methanone;
 - (1,4-diazabicyclo[3.2.2]non-4-yl)(4-phenylfuran-2-yl)methanone;
 - (1,4-diazabicyclo[3.2.2]non-4-yl)(4-(2-pyridyl)furan-2-yl)methanone;
 - (1,4-diazabicyclo[3.2.2]non-4-yl)(4-(3-pyridyl)furan-2-yl)methanone;
 - (1,4-diazabicyclo[3.2.2]non-4-yl)(4-(4-pyridyl)furan-2-yl)methanone;
- 20 (1,4-diazabicyclo[3.2.2]non-4-yl)(4-(furan-2-yl)furan-2-yl)methanone;
 - (1,4-diazabicyclo[3.2.2]non-4-yl)(4-(furan-3-yl)furan-2-yl)methanone;
 - (1,4-diazabicyclo[3.2.2]non-4-yl)(4-(thiophen-2-yl)furan-2-yl)methanone;
 - (1,4-diazabicyclo[3.2.2]non-4-yl)(4-(thiophen-3-yl)furan-2-yl)methanone;
 - (1,4-diazabicyclo[3.2.2]non-4-yl)(5-phenylthiophen-2-yl)methanone;
- 25 (1,4-diazabicyclo[3.2.2]non-4-yl)(5-(2-pyridyl)thiophen-2-yl)methanone;
 - (1,4-diazabicyclo[3.2.2]non-4-yl)(5-(3-pyridyl)thiophen-2-yl)methanone;
 - (1,4-diazabicyclo[3,2,2]non-4-yl)(5-(4-pyridyl)thiophen-2-yl)methanone;
 - (1,4-diazabicyclo[3.2.2]non-4-yl)(5-(furan-2-yl)thiophen-2-yl)methanone;
 - (1,4-diazabicyclo[3.2.2]non-4-yl)(5-(furan-3-yl)thiophen-2-yl)methanone;
- 30 (1,4-diazabicyclo[3.2.2]non-4-yl)(5-(thiophen-2-yl)thiophen-2-yl)methanone;
 - (1,4-diazabicyclo[3.2.2]non-4-yl)(5-(thiophen-3-yl)thiophen-2-yl)methanone;
 - (1,4-diazabicyclo[3.2.2]non-4-yl)(2-phenylfuran-4-yl)methanone;

- (1,4-diazabicyclo[3.2.2]non-4-yl)(2-(2-pyridyl)furan-4-yl)methanone;
- (1,4-diazabicyclo[3.2.2]non-4-yl)(2-(3-pyridyl)furan-4-yl)methanone;
- (1,4-diazabicyclo[3.2.2]non-4-yl)(2-(4-pyridyl)furan-4-yl)methanone;
- (1,4-diazabicyclo[3.2.2]non-4-yl)(2-(furan-2-yl)furan-4-yl)methanone;
- 5 (1,4-diazabicyclo[3.2.2]non-4-yl)(2-(furan-3-yl)furan-4-yl)methanone;
 - (1,4-diazabicyclo[3.2.2]non-4-yl)(2-(thiophen-2-yl)furan-4-yl)methanone;
 - (1,4-diazabicyclo[3.2.2]non-4-yl)(2-(thiophen-3-yl)furan-4-yl)methanone;
 - (1,4-diazabicyclo[3.2.2]non-4-yl)(4-phenylthiophen-2-yl)methanone;
 - (1,4-diazabicyclo[3.2.2]non-4-yl)(4-(2-pyridyl)thiophen-2-yl)methanone;
- 10 (1,4-diazabicyclo[3.2.2]non-4-yl)(4-(3-pyridyl)thiophen-2-yl)methanone;
 - (1,4-diazabicyclo[3.2.2]non-4-yl)(4-(4-pyridyl)thiophen-2-yl)methanone;
 - (1,4-diazabicyclo[3.2.2]non-4-yl)(4-(furan-2-yl)thiophen-2-yl)methanone;
 - (1,4-diazabicyclo[3.2.2]non-4-yl)(4-(furan-3-yl)thiophen-2-yl)methanone;
 - (1,4-diazabicyclo[3.2.2]non-4-yl)(4-(thiophen-2-yl)thiophen-2-yl)methanone, or
- 15 (1,4-diazabicyclo[3.2.2]non-4-yl)(4-(thiophen-3-yl)thiophen-2-yl)methanone, or a diastereoisomer, enantiomer or pharmaceutically-acceptable salt thereof.
 - 16. A compound according to any one of Claims 1 to 15, for use in therapy.
- 20 17. A compound according to any one of Claims 1 to 15, for use as a medicament.
- 18. Use of a compound as defined in any one of claims 1 to 15, in the manufacture of a medicament for the treatment or prophylaxis of psychotic disorders, intellectual impairment disorders, human diseases or conditions in which activation of the α7 nicotinic receptor is
 25 beneficial, Alzheimer's disease, learning deficit, cognition deficit, attention deficit, memory loss, Lewy Body Dementia, Attention Deficit Hyperactivity Disorder, anxiety, schizophrenia, mania or manic depression, Parkinson's disease, Huntington's disease, Tourette's syndrome, neurodegenerative disorders in which there is loss of cholinergic synapse, jetlag, cessation of smoking, nicotine addiction including that resulting from exposure to products containing
 30 nicotine, pain, ulcerative colitis or irritable bowel syndrome.

WO 2004/016617 PCT/SE2003/001277

-38-

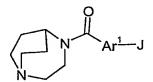
19. A method of treatment or prophylaxis of psychotic disorders, intellectual impairment disorders, human diseases or conditions in which activation of the α7 nicotinic receptor is beneficial, Alzheimer's disease, learning deficit, cognition deficit, attention deficit, memory loss, Lewy Body Dementia, Attention Deficit Hyperactivity Disorder, anxiety, schizophrenia, mania or manic depression, Parkinson's disease, Huntington's disease, Tourette's syndrome, neurodegenerative disorders in which there is loss of cholinergic synapse, jetlag, cessation of smoking, nicotine addiction including that resulting from exposure to products containing nicotine, pain, or ulcerative colitis which method comprises administering a therapeutically effective amount of a compound as defined in any one of Claims 1 to 15.

10

5

- 20. A pharmaceutical composition comprising a compound of formula I, as defined in any one of claims 1 to 15, together with at least one pharmaceutically-acceptable excipient or diluent.
- 15 21. A process for the preparation of a compound of formula I, as defined in any one of claims 1 to 15, which comprises:

reacting a compound of formula VI:



Vī

VI

wherein J represents halogen, or OSO₂CF₃ substituent at the position of ring Ar¹ at which the bond to ring Ar² is formed with a organometallic compound of formula VII;

in the presence of a organometallic catalyst and solvent.

22. A compound of formula VI:

25

20

wherein:

WO 2004/016617 PCT/SE2003/001277

-39-

Ar¹ is a benzene, furan, or thiophene ring;

J is halogen, or OSO₂CF₃, provided that when Ar¹ is a benzene ring, J may only represent halogen or OSO₂CF₃ in a position meta or para to the carboxamide group; or an enantiomer thereof or pharmaceutically-acceptable salts thereof.

5

- 23. A compound according to Claim 22, selected from:
 - (1,4-diazabicyclo[3.2.2]non-4-yl)(5-bromofuran-2-yl)methanone;
 - (1,4-diazabicyclo[3.2.2]non-4-yl)(5-bromothiophen-2-yl)methanone;
 - (1,4-diazabicyclo[3.2.2]non-4-yl)(3-bromophenyl)methanone;
- 10 (1,4-diazabicyclo[3.2.2]non-4-yl)(4-bromophenyl)methanone;
 - (1,4-diazabicyclo[3.2.2]non-4-yl)(3-iodophenyl)methanone;
 - (1,4-diazabicyclo[3.2.2]non-4-yl)(4-iodophenyl)methanone;
 - (1,4-diazabicyclo[3.2.2]non-4-yl)(4-bromothiophen-2-yl)methanone;
 - (1,4-diazabicyclo[3.2.2]non-4-yl)(5-bromothiophen-3-yl)methanone;
- 15 (1,4-diazabicyclo[3.2.2]non-4-yl)(5-bromofuran-2-yl)methanone;
 - (1,4-diazabicyclo[3.2.2]non-4-yl)(5-bromofuran-2-yl)methanone, and
 - (1,4-diazabicyclo[3.2.2]non-4-yl)(5-bromofuran-2-yl)methanone; or enantiomers thereof, or pharmaceutically-acceptable salts thereof.